

Applicant : Craig C. Mello et al.
Serial No. : 09/689,992
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Attorney's Docket No.: 07917-105001 / UMMC 00-04

REMARKS

Applicant hereby submits that the enclosures fulfill the requirements under 37 C.F.R. § 1.821-1.825. The amendments in the specification merely insert the paper copy of the Sequence Listing and sequence identifiers in the specification. I hereby state that this submission, filed in accordance with 37 CFR §1.821(g), does not contain new matter.

Attached hereto is a marked-up version of the changes made to the specification and claims by the current amendment.

Please apply any charges or credits to Deposit Account No. 06-1050.

Respectfully submitted,

Date: June 18, 2001

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"Version With Markings to Show Changes Made"

In the specification:

Paragraph beginning at page 7, line 30, has been amended as follows:

Figure 4B is an illustration of the predicted sequence of RDE-1 and its alignment with four related proteins. The sequences are RDE-1 (*C. elegans*; Genbank Accession No. AF180730; SEQ ID NO:3), F48F7.1 (*C. elegans*; Genbank Accession No. Z69661; SEQ ID NO:9), eIF2C (rabbit; Genbank Accession No. AF005355; SEQ ID NO:10), ZWILLE (*Arabidopsis*; Genbank Accession No. AJ223508; SEQ ID NO:6), and Sting (*Drosophila*; Genbank Accession No. AF145680; SEQ ID NO:7). Identities with RDE-1 are shaded in black, and identities among the homologs are shaded in gray.

Paragraph beginning at page 9, line 6, has been amended as follows:

Figure 11 is a depiction of regions of homology between the predicted RDE-4 amino acid sequence (SEQ ID NO:14), X1RBPA (SEQ ID NO:[6]11), HsPKR (SEQ ID NO:[7]12), and a consensus sequence (SEQ ID NO:8 and 15). A predicted secondary structure for RDE-4 is also shown illustrating predicted regions of helix and pleated sheet.

Paragraph beginning at page 47, line 14, has been amended as follows:

Analysis of the *rde-4* nucleic acid sequence shows that it encodes a protein (RDE-4) with similarities to dsRNA binding proteins. Examples of the homology to X1RBPA (SEQ ID NO:[6]11; Swissprot: locus TRBP_XENLA, accession Q91836; Eckmann and Jantsch, 1997, J. Cell Biol. 138:239-253) and HSPKR (SEQ ID NO:[7]12; AAF13156.1; Xu and Williams, 1998, J. Interferon Cytokine Res. 18:609-616), and a consensus sequence (SEQ ID NO:8 and 15) are shown in Fig. 11. Three regions have been identified within the predicted RDE-4 protein corresponding to conserved regions found in all members of this dsRNA binding domain family. These regions appear to be important for proper folding of the dsRNA binding domain. Conserved amino acid residues, important for interactions with the backbone of the dsRNA helix, are found in all members of the protein family including RDE-4 (see consensus residues in Figure 11). This motif is thought to provide for general non-sequence-specific interactions with

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dsRNA. The RDE-4 protein contains conserved protein folds that are thought to be important for the assembly of the dsRNA binding domain in this family of proteins. Conserved amino acid residues in RDE-4 are identical to those that form contacts with the dsRNA in the crystal structure of the X1RBP dsRNA complex. These findings strongly suggest that RDE-4 is likely to have dsRNA binding activity.